

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
14 March 2002 (14.03.2002)

PCT

(10) International Publication Number  
**WO 02/21144 A1**

(51) International Patent Classification<sup>7</sup>: **G01N 35/02,**  
**B01L 3/00**

(21) International Application Number: **PCT/SE01/01930**

(22) International Filing Date:  
7 September 2001 (07.09.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
0021987.3 7 September 2000 (07.09.2000) GB

(71) Applicant (for all designated States except US): **ASTRAZENECA AB** [SE/SE]; S-151 85 Södertälje (SE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **HARPER, Paul,**  
**Spencer** [GB/GB]; Affordable Automation Ltd., Unit  
21, The Bridgewater Centre, Robson Avenue, Urmston,  
Manchester M41 7TE (GB). **CALDWELL, Michael**

[GB/GB]; Affordable Automation Ltd., Unit 21, The  
Bridgewater Centre, Robson Avenue, Urmston, Man-  
chester M41 7TE (GB). **EVANS, Antony** [GB/GB];  
Affordable Automation Ltd., Unit 21, The Bridgewater  
Centre, Robson Avenue, Urmston, Manchester M41 7TE  
(GB). **FARNER, Lee** [GB/GB]; Affordable Automation  
Ltd., Unit 21, The Bridgewater Centre, Robson Avenue,  
Urmston, Manchester M41 7TE (GB).

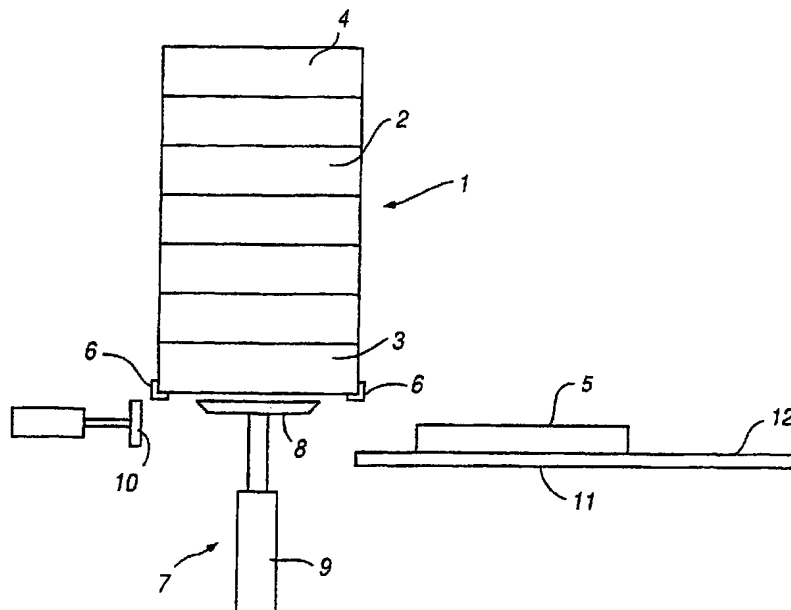
(74) Agent: **ASTRAZENECA AB**; Global Intellectual Prop-  
erty, S-151 85 Södertälje (SE).

(81) Designated States (national): AE, AG, AL, AM, AT, AU,  
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,  
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,  
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,  
MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI,  
SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU,  
ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM,  
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian

[Continued on next page]

(54) Title: PLATE HANDLING MECHANISM



(57) Abstract: A mechanism for removing a plate from a cassette of vertically stacked series of plates, for example microtitre palest is provided. The stack is confined within vertical members and the mechanism comprising means to grip the lower surface of the plate to be removed; means to lower the plate to be removed whilst it is gripped; means to support the remaining stack of plates; and means to translate the plate to be removed away from the remaining stack of plates; and means to translate the plate to be removed away from the remaining stack of plates. A method of removing the bottom plate of a stack of plates is provided, as is a method of analyzing compounds using the mechanism or method.

WO 02/21144 A1



patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

**Published:**

— with international search report

## PLATE HANDLING MECHANISM

This invention relates to a mechanism for providing a plate from a stack or cassette thereof.

5 The plates may particularly, but not exclusively, be of the type, which consist of planar object, which have a series of indents therein. Herein the term plate is held to include plates, trays and other planar objects, which can be separately manipulated. These objects may or may not have a series of indents therein. They may, for example, have traces of substance smeared on the surface thereof. They may contain indents, which are used to  
10 hold other containers such as small test tubes. The indents or test tubes may be used to contain compounds.

Such plates may be provided in a stack, which consists of a number of vertically arranged plates. Such stacks may be confined by means of vertical members to ensure that the stack  
15 is stable. Such a stack may be termed a cassette or cartridge. It is also known to provide an associated movement mechanism to enable one or more of the plates to be removed from and returned to a stack. Such stacks and their associated movement mechanism are widely employed in high throughput screening equipment utilized in the drug discovery process. It will be obvious to one skilled in the art to which the invention relates that the  
20 cassettes may be utilized for other purposes.

In the case of high throughput screening the plates may be known as microtitre plates. Such plates are available in 96, 384 and 1536 well versions. Stacks comprises a variable number of plates but generally do not exceed 50 in number.

There are a number of cassette stacks and cassette stack mechanisms available. The intention of such devices is to provide for the storage of cassettes when they are not being utilized, for example, in high throughput testing, when then are waiting for the compounds contained therein to be tested, or when the compounds have been tested. However these are  
5 passive systems in that that merely provide means for confining a stack of cassettes and allowing the removal of a particular cassette. The cassette is not actively ejected from the stack. In known mechanisms a separate return stack is provided for the used or returned cassettes. That is the cassettes are provided initially in a first stack and finish, at least intermenly, in a second stack. A further operation is required to return the cassettes to their  
10 original stack. This is, of course time, consuming and provides additional opportunities for errors or breakdowns to occur.

The form of the stack and the mechanism vary by manufacturer type, in details such as the number of cassettes provide and the exact form of support for the stack, but are all based  
15 on the requirement of a separate out and return stacks. In some known forms the stacks are provided as cartridges, that is a stack can be handled as a unit. For example a cartridge may allow a used stack to be removed and replaced by an unused one. In this system as in all current systems an empty stack or cartridge must be provided to allow used cassettes or cassettes which are not required to be positioned at least as an interim measure. This, of  
20 course, requires additional space.

Known forms of stack and stack mechanism passively download a cassette under gravity, that is a cassette in removed from the bottom of a stack, usually by means of a slot provided in vertical members which confine the cassettes. The cassettes are returned to the top of a separate stack, that is the are merely dropped onto another stack. It will be

appreciated that in cases as mentioned above an interim stack is used a cassette maybe dropped onto a stack containing none or few cassettes. In this case there is opportunity for the dropped cassette to misalign as it falls.

- 5 As mentioned above there are several potential problems with known mechanisms these can be summarised as follows. There is an additional space requirement due to the need for 2 stacks. Down stack errors occur causing system failure, caused by the adhesion of two plates in a stack and imprecise location of plates being lowered from the stacker. Up stack errors due to the mechanical force required to lift the weight in the return stack. Stacks are  
10 merely plugged into the stacker mechanism, allowing the entire cartridge to be forced out under load. Upon completion of a cassette content, the order of plates is reversed in the output requiring a restack back to the original order.

- In a number of known systems, particularly, but not solely high throughput compound  
15 testing systems a robot or robot arm is used to remove or dispense a plate from a stack, optionally, move the plate to a test location and return the plate to either an interim or a final destination.

A known such robotic system is the CRS F3 robot.

- 20 Robotic arm systems generally interface with a carousel where each plate is held separately on a shelf to remove these reliability problems, but they require time to load, often by hand, and use a large footprint. Known plate holding cassettes include one produced by Carl Creative Systems (Packard Bio-instruments).

According to the invention there is provided a mechanism for removing a plate from a cassette of vertically stacked series of plates, the stack being confined within vertical members the mechanism comprising means to grip the lower surface of the plate to be removed; means to lower the plate to be removed whilst it is gripped; means to support the  
5 remaining stack of plates; and means to translate the plate to be removed away from the remaining stack of plates.

Advantageously the stack of plates is of the microtitre type.

10 Preferably the means to grip the lower surface of the plate comprises a vacuum.

Preferably the means to translate the plate comprises a pneumatic ram.

Preferably the means to support the remaining plates comprises a catch.

15

Preferably the plate to be removed is translated to a location where the plate is processed.

Alternatively the plate is translated to a location where it is further moved by for example by means of a robot.

20

Preferably the removed plate is returned to the top of the remaining stack.

The present invention may also be said to consist in a high throughput compound tester wherein plates having a plurality of compounds to be tested are provided in a stack, the

stack being confined within vertical members, the tester including a mechanism comprising means to grip the lower surface of the plate to be removed; means to lower the plate to be removed whilst it is gripped; means to support the remaining stack of plates; and means to translate the plate to be removed away from the remaining stack of plates.

5

Advantageously the stack of plates is of the microtitre type.

Preferably the means to grip the lower surface of the plate comprises a vacuum.

10 Preferably the means to translate the plate comprises a pneumatic ram.

Preferably the means to support the remaining plates comprises a catch.

Preferably the plate to be removed is translated to a location where the compounds on the  
15 plate are tested.

Alternatively the plate is translated to a location where it is further moved by for example by means of a robot.

20 Preferably the removed plate is returned to the top of the remaining stack.

The present invention may also be said to consist in a high throughput compound tester wherein plates having a plurality of compounds to be tested are provided in a stack, the stack being confined within vertical members, the tester including a mechanism

comprising means to grip the lower surface of the plate to be removed; means to lower the plate to be removed whilst it is gripped; means to support the remaining stack of plates; means to translate the plate to be removed away from the remaining stack of plates and means to return the plate to the top of the remaining stack of plates.

5

The present invention may also be said to comprise a method of removing a microtitre plate from a cassette of vertically stacked series of such microtitre plates, the method comprising the steps of: gripping the lower surface of the microtitre plate to be removed; lowering the plate to be removed whilst it is gripped; supporting the remaining stack of microtitre plates; and translating the plate to be removed away from the remaining stack of microtitre plates.

Preferably the method of removing a microtitre plate further comprising the step of translating the removed microtitre plate to a location where the plate is processed.

To allow a better understanding, a mechanism, which embodies the present invention, will now be described by way of non-limitative example with reference to the accompanying drawings in which:

Figure 1 shows a side elevation of one preferred form of the present invention;

Figure 2 shows a front fragmentary elevation of another preferred form of the present invention;

Figure 3 shows a fragmentary back elevation of the form of the invention as shown in figure 2; and

5 Figure 4 shows a fragmentary side elevation of the form of the invention as shown in figures 2 and 3.

In the preferred form of the invention 1 as shown in figure 1 a stack 2 is provided of plates. The plates, for example 3, 4 and 5 may in particular but not exclusively, be of the type,  
10 which consist of planar objects, which have a series of indents therein. Herein the term plate is held to include plates, trays and other planar objects, which can be separately manipulated. These objects may or may not have a series of indents therein. They may, for example, have traces of substance smeared on the surface thereof. They may contain indents, which are used to hold other containers such as small test tubes. The indents or test  
15 tubes may be used to contain compounds or other substances, which are to tested or otherwise, processed.

Such plates are provided in a stack 2, which consists of a number of vertically arranged plates 3 and 4 plus, the unlabelled, but illustrated intermediate plates. Such stacks 2 may  
20 be confined by means of vertical members (not illustrated in figure 1 for the purposes of clarity) to ensure that the stack 2 is stable. Such a stack may be termed a cassette or cartridge. Such stacks 2 and their associated movement mechanism are widely employed in high throughput screening equipment utilized in the drug discovery process. It will be

obvious to one skilled in the art to which the invention relates that the cassettes may be utilized for other purposes.

The first preferred form of the invention provides means 6 to support the lower surface of the stack 2. Such means 6 may consist of a catch or a hinged member which supports the one two or more lower edges of the lowest plate 3 in the stack 2. The purpose of the means 6 is to support the lower most plate 3 and hence the stack to ensure that it does not translate vertically. It must however allow the lower most plate 3 to be removed when it is desired to do so.

Means 7 are always provided to grip or hold the lower most plate 3 and to translate it vertically downwards. The means 7 consists of means to grip the lower most surface of the lower most plate 3, in this case consisting of a planar member 8 having a vacuum therein. The member 8 is placed in contact with the lower surface of the lower most plate 3 and the vacuum draws the surface to the member thus gripping the lower most plate 3. The member 8 is translated by means of a pneumatic ram 9. The ram 9 provides vertical movement of the member both to allow it to rise into contact with the lower most surface of the lower most plate 3 and to lower the plate 3 (once the means 6 to support the lower surface of the stack is released).

Means 10 to translate the lower most plate 3 are also provided. In a preferred form of the invention such means comprises a pneumatic ram which simply pushes or translates the plate to be removed or lower most plate 3 away from the stack of plates 2. The plate to be removed or lower most plate slides along supporting means 11 to a distal end 12 thereof.

At the distal end 12 the compounds which are preferably present on the plate 3 maybe subjected to testing. However the plate 3 is preferably further dealt with at the distal end 12, for example a robot maybe utilised to further move the plate 3 to a different location at which the compounds present on the plate are tested or otherwise dealt with. In the most preferred form of the invention once the plate 3 has been dealt with it is returned to the top 4 of the stack 2. The need for a second interim stack is thus eliminated.

Figures 2 to 4 show another preferred form of the present invention in which means 13 are provided to contain the stack 2 and thus improve stability. Such means 13 may comprise vertical members, which align the stack 2 but allow individual plates to move vertically downwards as required.

In, at least, a preferred form of the present invention:

- 1) A single cassette or stack of plates 2 are used with a down stack for access, followed by the return of the plate 3 to the top 4 of the stack 2 by the robot.
- 2) Because the mechanism cycles plates within a stack 2 the plate order is maintained.
- 3) The incorporation of an air ram 8 to create a vacuum to grip the plate 3 and pull it out of the base of a stack 2 provides more control of the removal of a plate as opposed to allowing it to occur under the force of gravity.
- 4) The plate 3 is presented to the robot, which is preferably present, in a constant position 12
- 5) Plates are clamped to the mechanism by means 6 thus improving stability.

**CLAIMS**

- 1 A mechanism (1) for removing a microtitre plate (3) from a cassette of vertically stacked series (2) of such microtitre plates, the stack being confined within vertical members, the mechanism comprising: means (7) to grip the lower surface of the microtitre  
5 plate (3) to be removed; means to lower (9) the plate to be removed whilst it is gripped; means to support the remaining stack of microtitre plates; and means to translate the plate to be removed away from the remaining stack of microtitre plates.
- 10 2. A mechanism (1) for removing a microtitre plate (3) from a cassette of vertically stacked series (2) of such microtitre plates as claimed in claim 1 wherein the means (7) to grip the lower surface of the plate comprises a vacuum.
- 15 3. A mechanism (1) for removing a microtitre plate (3) from a cassette of vertically stacked series (2) of such microtitre plates as claimed in claim 1 or 2 wherein the means to translate the plate comprises a pneumatic ram (9).
- 20 4. A mechanism (1) for removing a microtitre plate (3) from a cassette of vertically stacked series (2) of such microtitre plates as claimed in any one of claims 1 to 3 wherein the means to support the remaining plates comprises a catch.
5. A mechanism (1) for removing a microtitre plate (3) from a cassette of vertically stacked series (2) of such microtitre plates as claimed in any one of claims 1 to 4 wherein the

removed microtitre plate (3) to be removed is translated (10) to a location where the plate is processed.

6. A mechanism (1) for removing a microtitre plate (3) from a cassette of vertically  
5 stacked series (2) of such microtitre plates as claimed in any one of claims 1 to 4 wherein the microtitre plate (3) is translated to a location where it is further processed by means of a robot.

7. A mechanism (1) for removing a microtitre plate (3) from a cassette of vertically stacked  
10 series (2) of such microtitre plates as claimed in any one of claims 1 to 6 wherein the removed plate is returned to the top of the remaining stacked series.

8. A high throughput compound tester wherein micrometer plates having a plurality of  
compounds to be tested thereon are provided as a series in a stack (2), the stack (2) being  
15 confined within vertical members, the tester including a mechanism comprising means (7) to grip the lower surface of the plate (3) to be removed; means to lower the plate to be removed whilst it is gripped; means to support the remaining stack of plates; means to translate the plate (3) to be removed away from the remaining stack of plates (2); means to test the compound(s) on said plate (3) and means to return the plate to the top of the  
20 remaining stack of plates.

9. A high throughput compound tester as claimed in claim 8 wherein the means (7) to grip the lower surface of the plate comprises a vacuum.

10. A high throughput compound tester as claimed in claim 8 or 9 wherein the means to translate the plate comprises a pneumatic ram (9).

11. A high throughput compound tester as claimed in any one of claims 8 to 10 wherein the  
5 means to support the remaining plates comprises a catch.

12. A high throughput compound tester as claimed in any one of claims 8 to 11 wherein the removed microtitre plate (3) to be removed is translated (10) to a location where the compound(s) on the plate are processed.

10

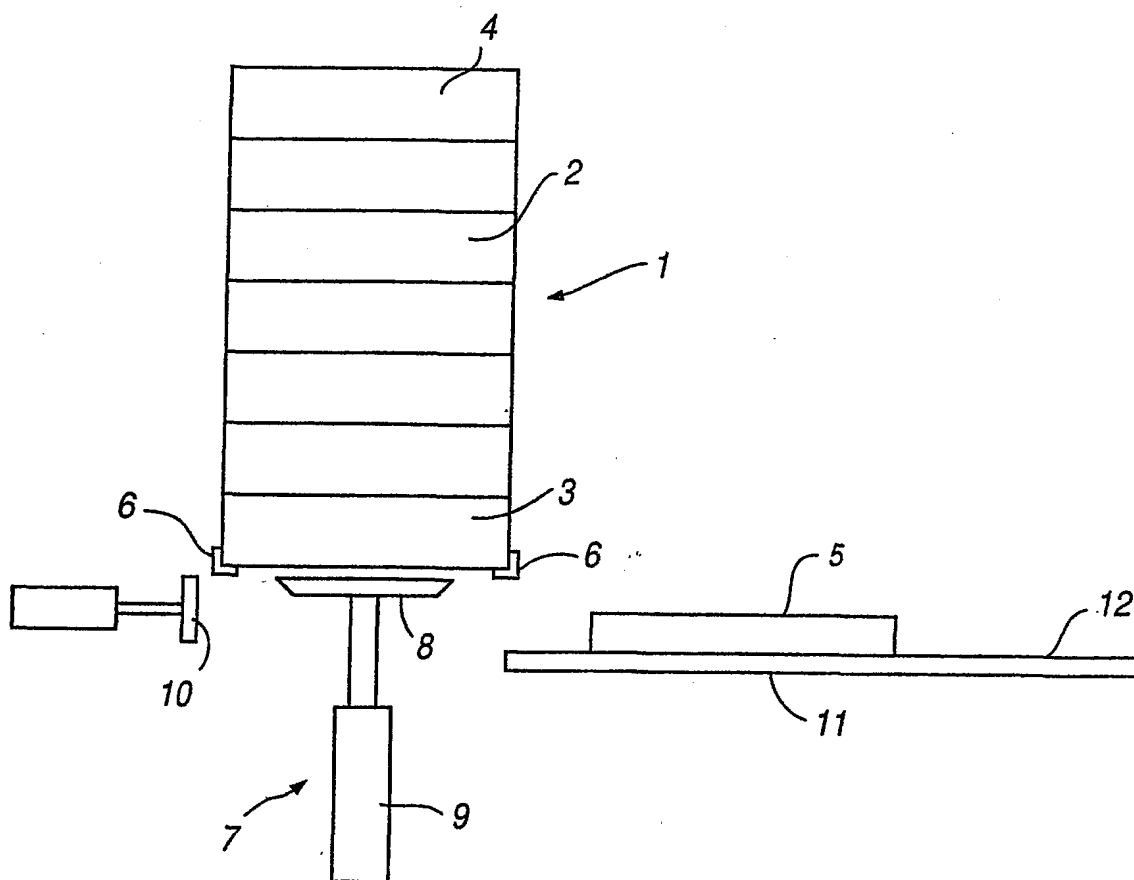
13. A method of removing a microtitre plate (3) from a cassette of vertically stacked series (2) of such microtitre plates, the method comprising the steps of: gripping the lower surface of the microtitre plate (3) to be removed; lowering (9) the plate to be removed whilst it is gripped; supporting the remaining stack of microtitre plates; and translating the  
15 plate to be removed away from the remaining stack of microtitre plates.

14. A method of removing a microtitre plate (3) from a cassette of vertically stacked series (2) of such microtitre plates as claimed in claim 13 wherein the gripping of the lower surface of the plate is by means of a vacuum.

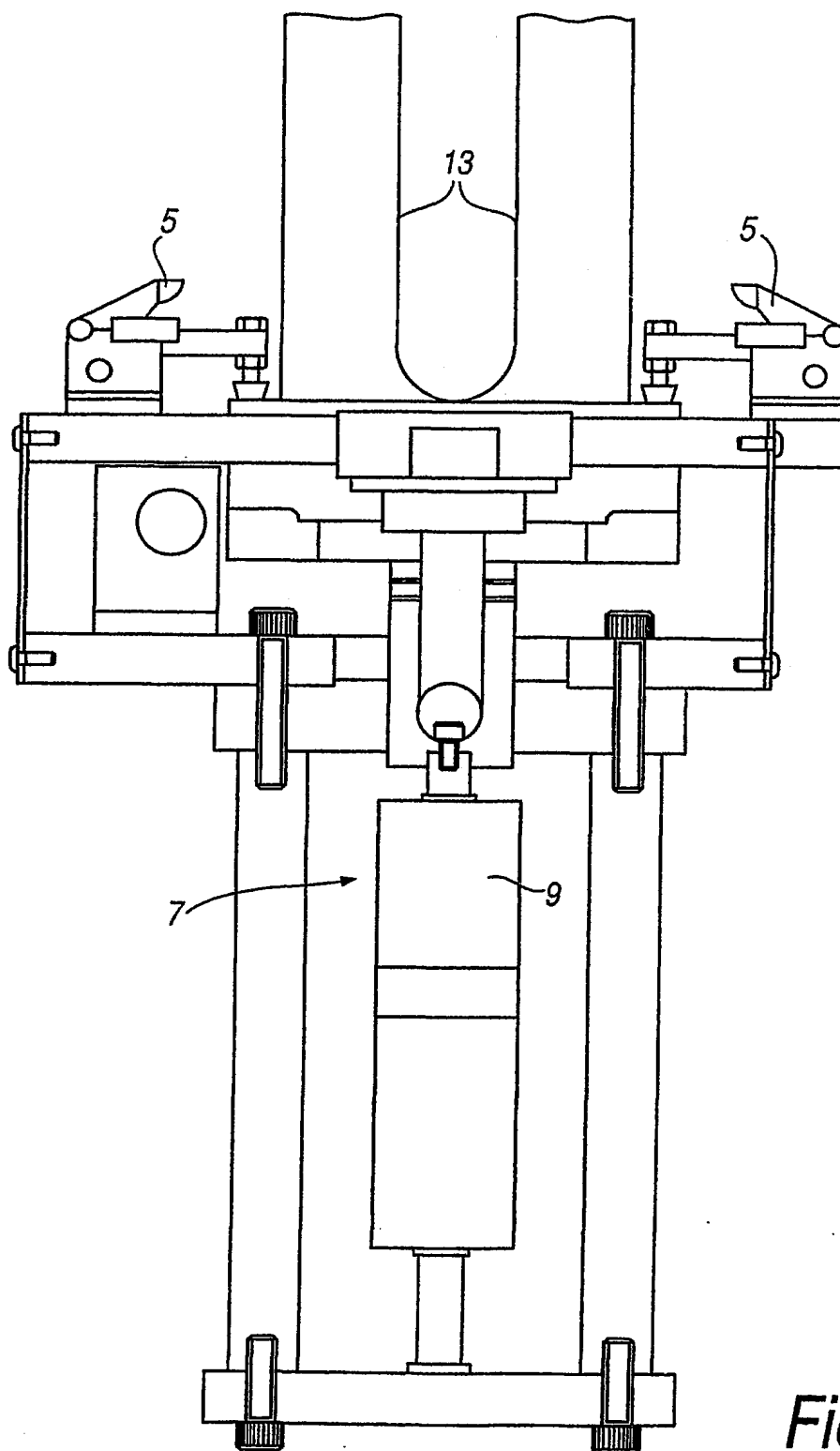
20

15. A method of removing a microtitre plate (3) from a cassette of vertically stacked series (2) of such microtitre plates as claimed in claim 13 or 14 further comprising the step of translating the removed microtitre plate (3) to a location where the plate is processed.

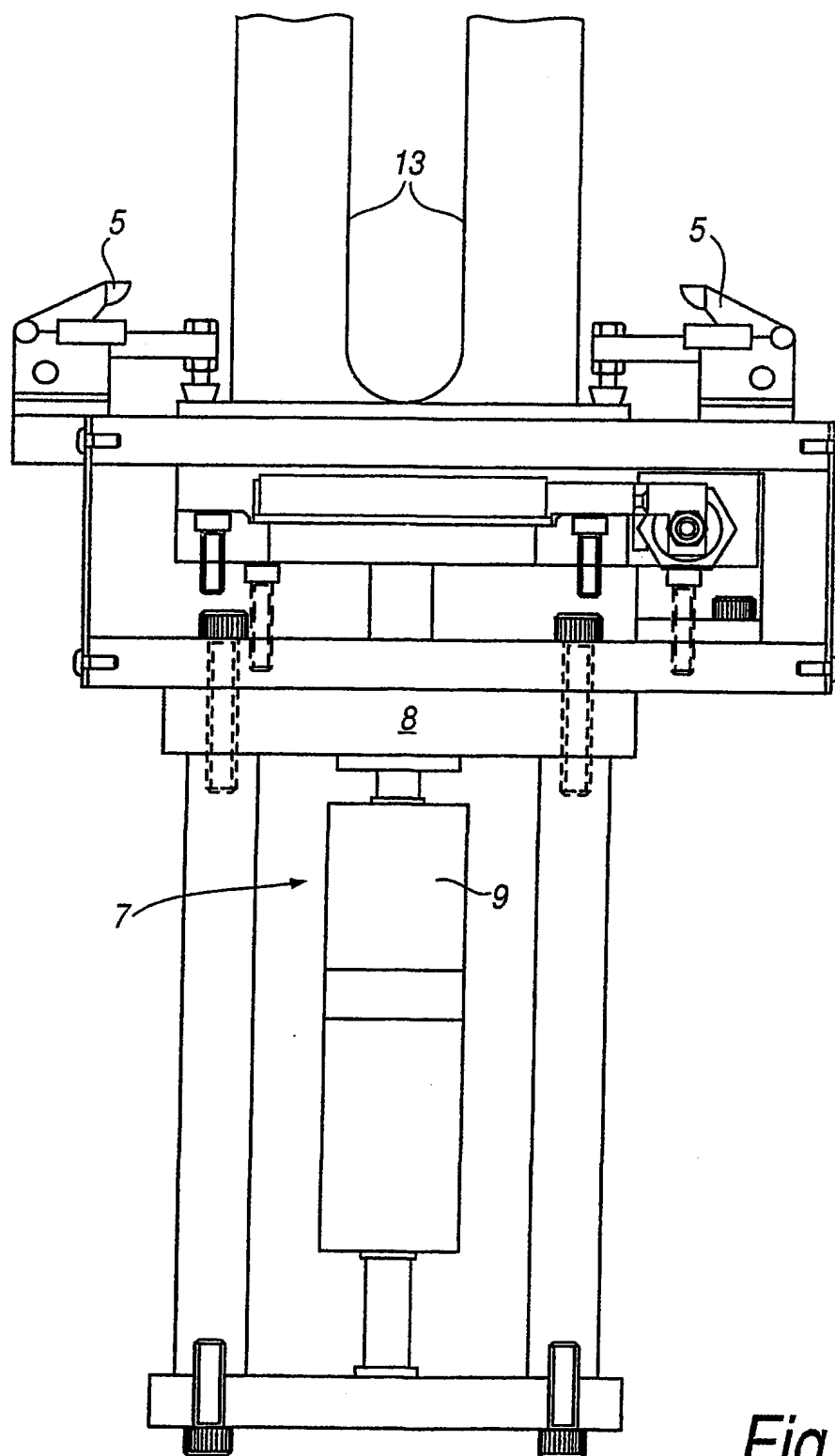
1/4

*Fig. 1*

2/4

*Fig.2*

3/4

*Fig. 3*

4/4

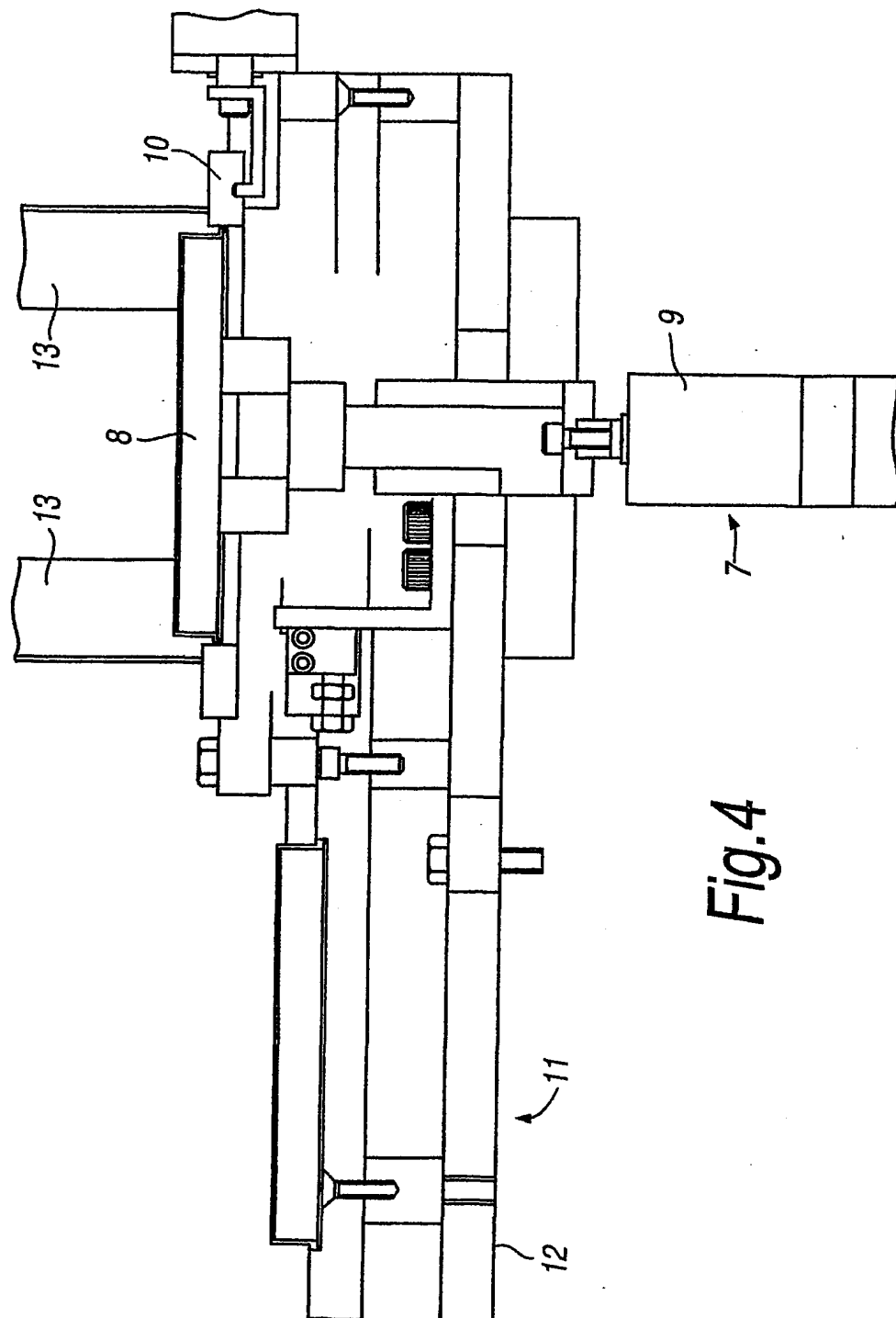


Fig.4

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/SE 01/01930

## A. CLASSIFICATION OF SUBJECT MATTER

IPC7: G01N 35/02, B01L 3/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: G01N, B01L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WPI

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5149654 A (J.GROSS ET AL), 22 Sept 1992 (22.09.92), column 2, line 36 - line 57	1,5,8,12-13, 15
A	--	2-4,6-7, 9-11,14
A	WO 9921016 A1 (JENOPTIK AKTIENGESELLSCHAFT), 29 April 1999 (29.04.99), abstract	1-15
A	GB 2225223 A (FLOW LABORATORIES LTD.), 30 May 1990 (30.05.90), claims 22-29, abstract	1-15
	--	

☒ Further documents are listed in the continuation of Box C.☒ See patent family annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&amp;" document member of the same patent family

Date of the actual completion of the international search

2 October 2001

Date of mailing of the international search report

19-12-2001

Name and mailing address of the ISA/

Swedish Patent Office

Box 5055, S-102 42 STOCKHOLM

Facsimile No. +46 8 666 02 86

Authorized officer

Mats Raidla /itw

Telephone No. +46 8 782 25 00

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/SE 01/01930

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4720463 A (G.FABER ET AL), 19 January 1988 (19.01.88), abstract  -----	1-15

Form PCT/ISA/210 (continuation of second sheet) (July 1998)

**INTERNATIONAL SEARCH REPORT**  
Information on patent family members

03/09/01

International application No.  
PCT/SE 01/01930

Patent document cited in search report			Publication date	Patent family member(s)		Publication date
US	5149654	A	22/09/92	AT	107192 T	15/07/94
				AU	624749 B	18/06/92
				AU	6673190 A	30/05/91
				CA	2030304 A	22/05/91
				DE	3938565 A	23/05/91
				DE	59006136 D	00/00/00
				EP	0429030 A,B	29/05/91
				SE	0429030 T3	
				ES	2056346 T	01/10/94
				JP	2874058 B	24/03/99
				JP	3183469 A	09/08/91
WO	9921016	A1	29/04/99	DE	19746455 C	27/05/99
				EP	0946881 A	06/10/99
GB	2225223	A	30/05/90	GB	8824499 D	00/00/00
				GB	8923599 D	00/00/00
US	4720463	A	19/01/88	CA	1273555 A	04/09/90
				DE	3686067 A,T	27/08/92
				EP	0193385 A,B	03/09/86
				JP	61247373 A	04/11/86
				US	4817785 A	04/04/89